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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/839,684	04/19/2001	Franklin Okumu	10466/18	1800

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EXAMINER
RUSSEL, JEFFREY E

ART UNIT	PAPER NUMBER
1654	11

DATE MAILED: 05/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/839,684	OKUMU, FRANKLIN	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 March 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Claims 1-52 are rejected under 35 U.S.C. 103(a) as being obvious over the European Patent Application 0 216 485 in view of Tipton et al (U.S. Patent No. 5,747,058). The European Patent Application '485 teaches compositions comprising a complex of a growth hormone and a metal, preferably zinc, in combination with a thickened oil vehicle comprising mineral oil or vegetable oil, and optionally in combination with adjuvants or excipients which further extend the release rate of the metal-complexed growth hormone. Preferred oil vehicles are mixtures of peanut oil and aluminum monostearate, and mixtures of soybean oil and beeswax. The molar ratio of zinc to growth hormone is at least 1:1, preferably at least 2:1. The compositions are injected or introduced into an animal as an implant. See, e.g., page 2, lines 20-23; page 3, lines 14-17; and page 3, line 24 - page 4, line 22. The European Patent Application '485 teaches the use of biocompatible thickened oil vehicles in general (see, e.g., page 3, lines 29-32, and claim 10), but does not teach Applicant's particularly claimed carrier material comprising sucrose acetate isobutyrate and a solvent. Tipton et al disclose high viscosity liquid controlled delivery systems comprising a component (HVLCM) that has a viscosity of at least 5,000 cP at 37°C and that does not crystallize neat under ambient or physiological conditions. A preferred component is sucrose acetate isobutyrate (SAIB). The delivery systems can include solvents such as ethanol, propylene carbonate, and benzyl alcohol, which lower the viscosity of the delivery system, e.g. to less than 1000 cP or less than 200 cP, for purposes of administration and which then dissipate or diffuse, leaving a highly viscous implant. Ratios of SAIB:solvent of 60:40 and of 70:30 are exemplified. By selection of the HVLCM and the solvent, a wide variety of pre-

and post-administration composition viscosities can be achieved. The delivery systems can be used for the controlled release delivery of substances such as natural and synthetic bioactive peptides and proteins, including growth factors. The substances to be delivered can preferably be present in amounts ranging from about 2 % to about 10% by weight. See, e.g., the Abstract; column 2, lines 47-67; column 8, lines 16-25 and 41-49; and column 14, lines 1-18. It would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to use the delivery system of Tipton et al as the biocompatible thickened oil vehicles of the European Patent Application '485 because the European Patent Application '485 is not limited to the use of any particular biocompatible thickened oil vehicle, because the delivery system of Tipton et al is disclosed to be useful in delivering the same types of biologically active substances, i.e. proteins including growth factors, which are disclosed by the European Patent Application '485, and because use of the delivery system of Tipton et al as the biocompatible thickened oil vehicle of the European Patent Application '485 would have the advantage of providing simple controlled delivery systems which are easily formulated and which provide different pre- and post-administration viscosities for ease of administration (see, e.g., column 2, lines 30-67). Neither the European Patent Application '485 nor Tipton et al teach the exact release rates recited in instant claims 27-30, 32-35, and 37-40. However, the European Patent Application '485 does teach that use of the metal complexes of growth hormone allows a slower release rate upon injection than does the free form of growth hormone (see page 2, lines 7-10), and Tipton et al disclose that release rates can be chosen and optimized by appropriate choice of additives (see column 3, lines 30-44, and column 9, lines 1-5). It would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to adjust the

composition of the delivery system in order to optimize the release rates of the European Patent Application '485 as modified above by Tipton et al because the European Patent Application '485 discloses the desirability of a slower release rate upon injection and because Tipton et al disclose that release rate is a result-effective variable and therefore one of ordinary skill in the art would be motivated to optimize such a variable.

3. Applicant's arguments filed March 27, 2003 have been fully considered but they are not persuasive.

The anticipation rejection over the European Patent Application 0 216 485 set forth in the previous Office action is withdrawn for the reasons given by Applicant in the response.

The obviousness rejection over the European Patent Application 0 216 485 in view of Tipton et al is maintained. Applicant contends that Figure 4 shows an unexpected decrease in initial burst for Applicants' compositions comprising multivalent metal cations rather than monovalent metal cations, in comparison to the European Patent Application '485's compositions comprising multivalent metal cations rather than no complexing metal cations. Applicant's argument is not persuasive because the showings discussed by Applicant in the response are not probative side-by-side comparisons with the prior art and are not commensurate in scope with the claims. Firstly, Applicant determines a reduction in initial burst for Applicant's invention by comparing zinc and sodium cations, whereas Applicant determines a reduction in initial burst for the European Patent Application '485's compositions by comparing zinc cations and the absence of metal cations. These are two different methods for determining reductions in initial burst, and it can not be concluded that any reduction in initial burst is due to Applicant's composition rather than the composition to which the comparisons are being made.

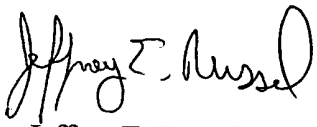
Secondly, Applicant appears to determine a reduction in initial burst for Applicant's compositions using an in vitro testing system (see, e.g., page 2, lines 33-35, of Applicant's specification), whereas the European Patent Application '485's reduction in initial burst is determined using an in vivo testing system (see, e.g., page 11, lines 1-11). The numerical values obtained for reductions in initial burst in in vitro and in vivo testing systems are not directly comparable. Thirdly, Applicants' specification does not appear to show what loading values and what metal cation:growth hormone ratios were used in the experiments which resulted in the data presented in Figure 4. Unless the loading values and hormone ratios were the same as those used in the compositions tested in the European Patent Application '485, it is not possible to conclude that any reduction in initial burst is due to the presence of a divalent metal cation such as zinc. Note that Applicant states at page 2, lines 35-36, of the specification that release rates vary widely depending upon the preparation being tested. Because Applicant's claims are not limited to any particular preparation or, with the exception of claims 27, 28, 32, 33, 37, and 38, to any particular initial burst, it can not be concluded that Applicant's claims are limited to compositions which possess the unexpected decrease in initial burst which Applicant argues is evidence of unexpected results. Finally, Applicant's initial burst tests as illustrated in Figure 4 are limited to Zn cations, whereas many of Applicants' claims are drawn to multivalent metal cations in general, and the European Patent Application '485 discloses the use of several multivalent cations other than zinc (see, e.g., page 3, lines 15-16). Again, the showing is not commensurate in scope with the rejected claims. The examiner maintains that the prima facie case of obviousness has not been rebutted by an appropriate showing of unexpected results.

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brenda Brumback can be reached at (703) 306-3220. The fax number for Art Unit 1654 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 746-5175 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.



Jeffrey E. Russel
Primary Patent Examiner
Art Unit 1654

JRussel
May 5, 2003